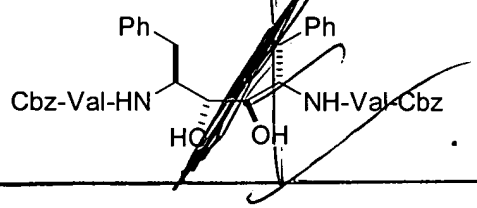
leucine-valine-, carbobenzyloxy-phenylalanine-valine-, carbobenzyloxy-serine-valine-, carbobenzyloxy-threonine-valine-, carbobenzyloxy-valine-valine- and carbobenzyloxy-alanine-asparagine-.

23. (new) A protease inhibitor represented by the following structure:




**Remarks**

Sequence ID No.'s:

In compliance with 37 CFR 1.821-1.825, Applicant submits a computer readable copy and a paper copy of the Sequence Listings for each of the amino acid and nucleic acid sequences employed in the Specification. The Specification has been amended, as indicated above, to include SEQ ID No.'s for each of the amino acid and nucleic acid sequences therein.

Priority Applications:

In compliance with 35 USC 119(e), the Specification has been amended to include a Cross-Reference to priority applications.

Rejection under 35 U.S.C. § 112, second paragraph:

Claims 6 and 8 have been rejected under 35 U.S.C. § 112, second paragraph, for indefiniteness. Claims 6 and 8 have now been amended so as to comply with the definiteness requirements of 35 U.S.C. § 112, second paragraph.

Rejection under 35 U.S.C. § 103(a):

Claim 1 is rejected under 35 U.S.C. § 103(a) as obvious over European Patent Application '145. Applicant traverses this rejection.

European Patent Application '145 teaches away from having any additional amino acids on the N-terminus of the "dipeptide." Indeed, the bulk of the compounds claimed by '145 possess an unnatural proline-like residue. The other naturally occurring proline residue found in nature, 4R-hydroxyproline, was not included in the list of analogs although this amino acid is readily available. Inclusion of proline is incidental and does not fit into the motif of their invention. These inventors specifically desired to have unnatural amino acids which would be resistant to peptidases found in the digestive tract. Capping the N-terminus of the "dipeptide" with an acyl group makes this compound even more resistant to digestive enzymes. Accordingly, European Patent Application '145 teaches against having residues or structures that might be subject to digestive enzymes, unlike the compounds of claim 1 in the instant application.

Rejection under 35 U.S.C. § 102(b):

Claim 2 is rejected under 35 U.S.C. § 102(b) as anticipated by WO Patent Application '361. This rejection has been obviated by Applicant's cancellation of Claim 2.

Rejection under 35 U.S.C. § 103(a):

Claim 2 is rejected under 35 U.S.C. § 103(a) as obvious over a reference by Baker et al. This rejection has been obviated by Applicant's cancellation of Claim 2.

Rejection under 35 U.S.C. § 102(b):

Claim 2 is rejected under 35 U.S.C. § 102(b) as anticipated by a reference by Dreyer et al. This rejection has been obviated by Applicant's cancellation of Claim 2.

Rejection under 35 U.S.C. § 103(a):

Claim 2 is rejected under 35 U.S.C. § 103(a) as obvious over a reference by Kempf et al. This rejection has been obviated by Applicant's cancellation of Claim 2.

Rejection under 35 U.S.C. § 103(a):

Claim 3 is rejected under 35 U.S.C. § 103(a) as obvious over a reference by Handa et al. Applicant traverses this rejection.

Claim 3 has been amended so as to require that the claimed protease inhibitor must be stereochemically pure. Handa et al. does not teach or enable stereochemically pure protease inhibitors. Support for the importance of stereochemistry is found in the Specification at Figure 2. The compounds of Claim 3 are also patentably unobvious over Handa, because there is no teaching or suggestion in the cited prior art that valine can be a functional equivalent of asparagine or cysteine in this context.

Rejection under 35 U.S.C. § 102(b):

Claim 4 is rejected under 35 U.S.C. § 102(b) as anticipated by a reference by Thompson et al. This rejection has been obviated by Applicant's cancellation of Claim 4.

Rejection under 35 U.S.C. § 102(b):

Claim 5 is rejected under 35 U.S.C. § 102(b) as anticipated by a reference by Tien et al. This rejection has been obviated by Applicant's cancellation of Claim 5.

Rejection under 35 U.S.C. § 102(b):

Claims 1, 6, and 8 are rejected under 35 U.S.C. § 102(b) as anticipated by a reference by Tam et al. Applicant traverses this rejection. Claims 1, 6, and 8 have been amended so as to avoid anticipation by Tam et al.

Rejection under 35 U.S.C. § 102(b):

Claim 1 is rejected under 35 U.S.C. § 102(b) as anticipated by a reference by WO Patent Application '100. Applicant traverses this rejection. Claim 1 has been amended so as to avoid anticipation by WO Patent Application '100.

Rejection under 35 U.S.C. § 103(a):

Claims 2, 10, and 11 (or possibly 2, 12, and 14) are rejected under 35 U.S.C. § 103(a) as obvious over a reference by WO Patent Application '948. Applicant traverses this rejection. Applicant's cancellation of Claim 2 obviates this rejection with respect to that claim. Examiner's basis for rejection is inapplicable to Claims 10 and 11. Possibly, Examiner meant to apply this rejection to Claims 12 and 14. Claims 12 and 14 have been amended to require that the claimed protease inhibitor be stereochemically pure. There is no suggestion in the cited prior art that these compounds should be stereochemically pure. Furthermore, there is no suggestion in the cite prior art that Val can substitute for Ala in this particular class of compounds. Steric considerations are known to be important for activity and unpredicable.

Rejection under 35 U.S.C. § 102(b):

Claims 2 and 10 are rejected under 35 U.S.C. § 102(b) as anticipated by a reference by Jadhav et al. Applicant traverses this rejection. Claim 2 has been cancelled; Claim 10 has been amended so as to require stereochemical purity. Amended Claim 10 avoids anticipation by Jadhav et al.

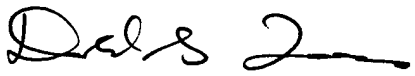
Rejection under 35 U.S.C. § 103(a):

Claim 11 is rejected under 35 U.S.C. § 103(a) as obvious over a reference by Jadhav et al. Applicant traverses this rejection. Claim 11 has been amended so as to require stereochemical purity. There is no suggestion in the cited prior art that stereochemical purity with respect to diols will enhance activity. Amended Claim 11 avoids being obvious over Jadhav et al.

Summary:

Applicant believes that Claims 1, 3, 6, 8, 10-19, and 21, as amended, and unamended Claims 7, 9, 20, and 22 are patentably novel and unobvious. Notice of Allowance of claims 1, 3, 6-22 is respectfully requested.

Respectfully submitted,



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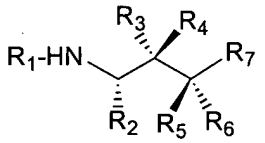
# APPENDIX

## VERSION OF CLAIMS WITH MARKINGS TO SHOW CHANGES MADE

A marked-up version of amended claims 1, 3, 6, 8, 10-19, and 21 showing the changes made are provided below. Claims 2, 4, and 5 have been cancelled without prejudice. Claims 7, 9, 20 and 22 are unamended. Claim 23 is new.

1. (once amended) A protease inhibitor represented by the following structure:




wherein

$R_1$ is selected from the group consisting of hydrogen, carbobenzyloxy-, [carbobenzyloxy-valine-,] carbobenzyloxy-glycine-valine-, carbobenzyloxy-alanine-valine-, carbobenzyloxy-leucine-valine-, carbobenzyloxy-phenylalanine-valine-, carbobenzyloxy-serine-valine-, carbobenzyloxy-alanine-asparagine-, carbobenzyloxy-threonine-valine- and carbobenzyloxy-valine-valine-;

$R_2$ is selected from the group consisting of $-CH_2$-Phenyl, and $-CH_2-CH(CH_3)_2$;

$R_3$ is selected from the group consisting of hydrogen, oxygen and hydroxyl; $R_4$ is selected from the group consisting of hydrogen, oxygen and hydroxyl, wherein $R_3$ and $R_4$ are not both hydroxyl and wherein $R_3$ and $R_4$ are either not oxygen or are a single combined oxygen forming a carbonyl group;

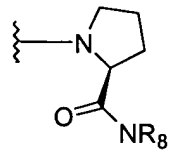
$R_5$ is selected from the group consisting of hydrogen, and oxygen; $R_6$ is selected from the group consisting of hydrogen, and oxygen, wherein $R_5$ and $R_6$ are either a single combined oxygen forming a carbonyl group or both seperately

# APPENDIX

## VERSION OF CLAIMS
## WITH MARKINGS TO SHOW CHANGES MADE

hydrogen;

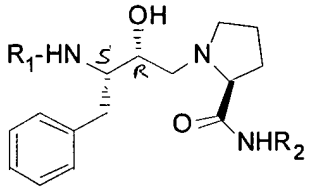
$R_7$ is a radical represented by the formula:



wherein $R_8$ is a radical selected from the group consisting of -$(H)_2$, and -H(t-Butyl); with a proviso that, if either $R_2$ or $R_3$ is hydroxyl, then $R_1$ is neither hydrogen nor carbobenzyloxy-.

2. (cancelled)

3. (once amended) A stereochemcially pure protease inhibitor represented by the following structure:



wherein

$R_1$ is a radical selected from the group consisting of hydrogen, carbobenzyloxy-, carbobenzyloxy-valine-, carbobenzyloxy-glycine-valine-, carbobenzyloxy-alanine-valine-, carbobenzyloxy-leucine-valine-, carbobenzyloxy-phenylalanine-valine-, carbobenzyloxy-serine-valine-, carbobenzyloxy-threonine-valine- , carbobenzyloxy-alanine-asparagine- and carbobenzyloxy-valine-valine-; and

$R_2$ is a radical selected from the group consisting of -$(H)_2$, and -H(t-Butyl).

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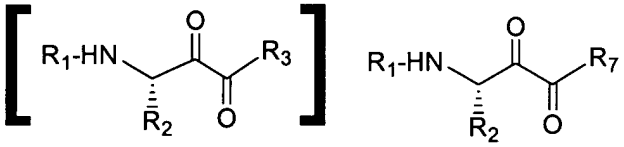
## VERSION OF CLAIMS
## WITH MARKINGS TO SHOW CHANGES MADE

4. (cancelled)

5. (cancelled)

6. (once amended) A protease inhibitor [according to Claim 1] represented by the following structure:

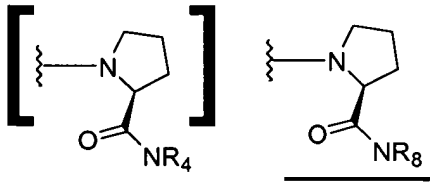


wherein

$R_1$ is selected from the group consisting of [hydrogen, carbobenzyloxy-, carbobenzyloxy-valine-,] carbobenzyloxy-glycine-valine-, carbobenzyloxy-alanine-valine-, carbobenzyloxy-leucine-valine-, carbobenzyloxy-phenylalanine-valine-, carbobenzyloxy-serine-valine-, carbobenzyloxy-alanine-asparagine-, carbobenzyloxy-threonine-valine- and carbobenzyloxy-valine-valine-;

$R_2$ is selected from the group consisting of $-CH_2$-Phenyl, and $-CH_2-CH(CH_3)_2$;

[$R_3$] $\underline{R_7}$ is a radical represented by the formula:



wherein [$R_4$] $\underline{R_8}$ is a radical selected from the group consisting of $-(H)_2$, and -H(t-Butyl).

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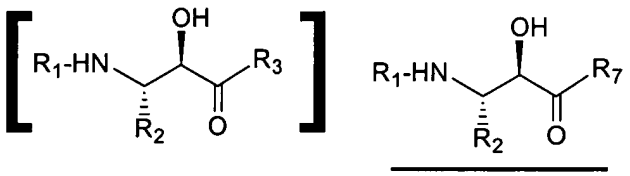
## VERSION OF CLAIMS
## WITH MARKINGS TO SHOW CHANGES MADE

8. (once amended) A protease inhibitor [according to Claim 1] represented by the following structure:

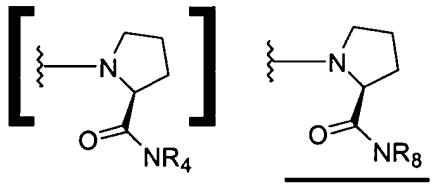


wherein

$R_1$ is selected from the group consisting of [carbobenzyloxy-valine-,] carbobenzyloxy-glycine-valine-, carbobenzyloxy-alanine-valine-, carbobenzyloxy-leucine-valine-, carbobenzyloxy-phenylalanine-valine-, carbobenzyloxy-serine-valine-, carbobenzyloxy-alanine-asparagine-, carbobenzyloxy-threonine-valine- and carbobenzyloxy-valine-valine-;

$R_2$ is selected from the group consisting of $-CH_2$-Phenyl, and $-CH_2-CH(CH_3)_2$;

[$R_3$] $\underline{R_7}$ is a radical represented by the formula:



wherein [$R_4$] $\underline{R_8}$ is a radical selected from the group consisting of $-(H)_2$, and -H(t-Butyl).

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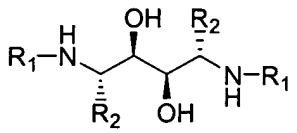
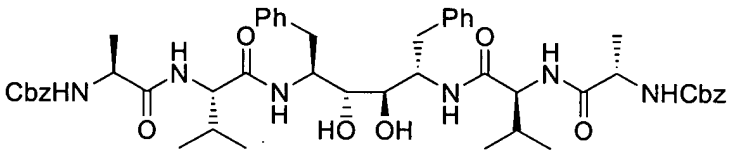
## VERSION OF CLAIMS
## WITH MARKINGS TO SHOW CHANGES MADE

10. (once amended) A stereochemically pure protease inhibitor [according to Claim 2] represented by the following structure:

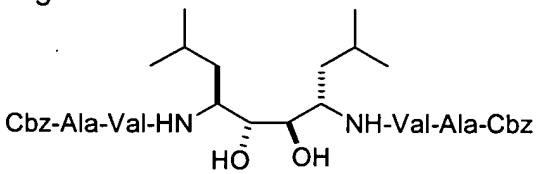


wherein $R_1$ is a radical selected from the group consisting of carbobenzyloxy-glycine-valine-, carbobenzyloxy-alanine-valine-, carbobenzyloxy-leucine-valine-, carbobenzyloxy-phenylalanine-valine-, carbobenzyloxy-serine-valine-, carbobenzyloxy-threonine-valine-, carbobenzyloxy-alanine-asparagine- and carbobenzyloxy-valine-valine-; $R_2$ is selected from the group consisting of $-CH_2$-Phenyl, and $-CH_2-CH(CH_3)_2$.

11. (once amended) A stereochemically pure protease inhibitor according to claim 10 represented by the following structure:



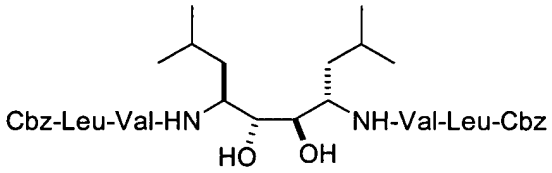
12. (once amended) A stereochemically pure protease inhibitor according to claim 10 represented by the following structure:



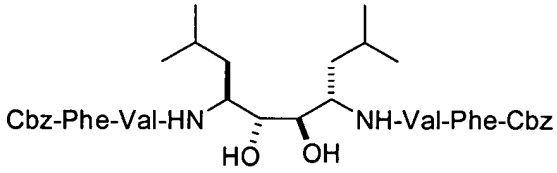
# APPENDIX

## VERSION OF CLAIMS
## WITH MARKINGS TO SHOW CHANGES MADE

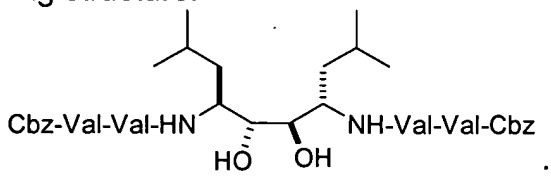
13. (once amended) A stereochemically pure protease inhibitor according to claim 10 represented by the following structure:



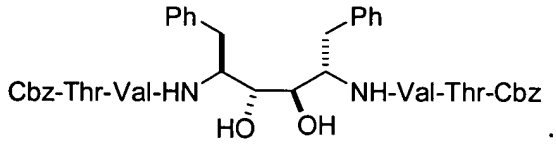

14. (once amended) A stereochemically pure protease inhibitor according to claim 10 represented by the following structure:




15. (once amended) A stereochemically pure protease inhibitor according to claim 10 represented by the following structure:




16. (once amended) A stereochemically pure protease inhibitor according to claim 10 represented by the following structure:



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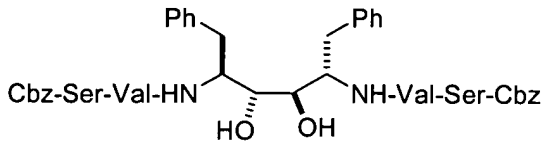
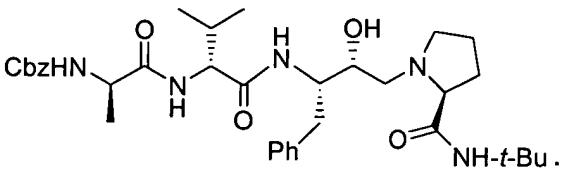
## VERSION OF CLAIMS WITH MARKINGS TO SHOW CHANGES MADE

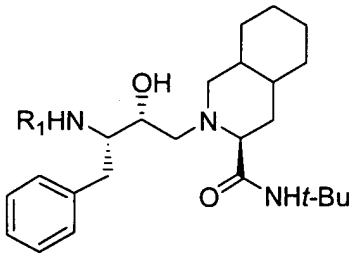
17. (once amended) A stereochemically pure protease inhibitor according to claim 10 represented by the following structure:




18. (once amended)A stereochemically pure protease inhibitor according to claim 3 represented by the following structure:




19. (once amended) A protease inhibitor [according to Claim 4] represented by the following structure:

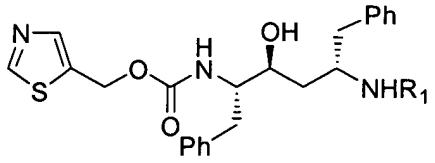



wherein $R_1$ is a radical selected from the group consisting of carbobenzyloxy-valine-, carbobenzyloxy-glycine-valine-, carbobenzyloxy-alanine-valine-, carbobenzyloxy-leucine-valine-, carbobenzyloxy-phenylalanine-valine-, carbobenzyloxy-serine-valine-, carbobenzyloxy-threonine-valine-, carbobenzyloxy-valine-valine- and carbobenzyloxy-alanine-asparagine-.

# APPENDIX

## VERSION OF CLAIMS
## WITH MARKINGS TO SHOW CHANGES MADE

21. (once amended) A protease inhibitor [according to Claim 5] represented by the following structure:




wherein $R_1$ is a radical selected from the group consisting of carbobenzyloxy-valine-, carbobenzyloxy-glycine-valine-, carbobenzyloxy-alanine-valine-, carbobenzyloxy-leucine-valine-, carbobenzyloxy-phenylalanine-valine-, carbobenzyloxy-serine-valine-, carbobenzyloxy-threonine-valine-, carbobenzyloxy-valine-valine- and carbobenzyloxy-alanine-asparagine-.

23. (new) A protease inhibitor represented by the following structure: